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LETTER TO THE EDITOR

Investigation of Excess Cancer of Other and Unspecified Sites Among Chemical Workers

Earlier, we reported finding an excess of mortality from cancer of other and unspecified sites among more than 37,000 past and present, male employees of Dow Chemical facilities in Midland and Bay City, Michigan [Bond et al., 1987]. A total of 169 deaths from other and unspecified cancer was observed compared to 125.3 expected (SMR = 135; 95% CI = 115–157). Herein, we report the results of a follow-up study designed to investigate several alternative explanations for the excess.

As used in the Monson [1974] lifetable analysis program, the category of "cancer of other and unspecified sites" (COUS) is a wastebasket for: 1) uncommon cancers of miscellaneous sites, e.g., "male breast"; 2) cancers specified as secondary, e.g., "lung cancer, primary site unknown" or, in some instances, not specified as primary, e.g., "liver cancer"; and 3) cancers of ill-defined or unspecified sites, e.g., "malignant mesothelioma." One possible explanation for the excess was that it was due to a greater than expected occurrence of one or more of the individual cancer sites that comprise the category.

We tested this by first separating the 41 death certificates coded to miscellaneous other sites from the 128 for which the cause of death was truly unspecified. Next, we calculated expected numbers of deaths using the NIOSH lifetable program [Waxweiler et al., 1983], which includes mortality rates for several of the individual cancer sites which are pooled together to form the COUS category in the Monson program. This revealed small non-statistically significant excesses for connective tissue cancer (11 observed vs. 7.3 expected, SMR = 151, 95% CI = 75–270), and male breast cancer (5 observed vs. 2.7 expected, SMR = 185, 95% CI = 60–432), and a slight deficit of liver cancer, unspecified as primary or secondary (10 observed vs. 14.2 expected, SMR = 70, 95% CI = 34–130).

Rates were not available from the NIOSH program to permit calculation of expected numbers of deaths from cancer of other endocrine glands (4 observed) and malignant mesothelioma (11 observed); however, the mesotheliomas undoubtedly represent an excess as was acknowledged in the original report [Bond et al., 1987].

We next considered the possibility that our nosologist was coding the death

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certificates without the benefit of any additional diagnostic information obtained by the State Offices of Vital Statistics through querying the certifying physician [Bond et al., 1982]. Not every certificate prompts a query, but unspecified cancers are among the diagnoses routinely queried by most states. Lacking the additional diagnostic information, our nosologist would arrive at a less-specific underlying cause of death code than the nosologists at the state level or the National Center for Health Statistics [NCHS, 1980].

We tested this second hypothesis by obtaining the underlying cause of death codes which had been assigned by the states' nosologists (and presumably accepted by NCHS) either directly from the death certificate itself (the codes were often handwritten on the document) or by special arrangement with the respective State Offices of Vital Statistics. We were successful in doing this for 92.9% of the total deaths, and found 12 instances in which the states' nosologist had coded the death to a specified cancer site; presumably based on the queried information. These 12 deaths were coded to specific cancer sites in the national and local mortality statistics, which formed the basis for our comparisons, but had been coded as unspecified cancers in our data set, thus introducing a differential misclassification bias.

That the certification practices of one or more local physicians could be responsible for a portion of the excess was considered to be yet another possible explanation. Subsequent to conducting our original cohort mortality study, we discovered that during 1970 to 1979 the death rate for COUS in neighboring Bay County was twice the national rate [Riggan et al., 1983].

Although we had incorporated a comparison of employee mortality with that of residents of seven East-Central Michigan counties, we had specifically excluded Bay County because of differing population characteristics. Nevertheless, approximately 16% of the current workforce reside there.

We undertook a nested case-control study to determine: 1) if Bay county residents were overrepresented among employee deaths from COUS; and 2) if there were any commonalities among the patients' physicians or hospitals. Two control groups were utilized, the first of which was comprised of the 7,635 deaths from specified causes, and the second of the 1,549 deaths from cancers of specified sites. County of residence at time of death, physician, and hospital name were abstracted from the death certificates, and odds ratios were calculated both unadjusted and adjusted for age and year of death [Mantel and Haenszel, 1959].

A statistically significant two-fold risk (95% CI = 1.3–2.8) was found for having been a resident of Bay County, and was unaffected by the choice of control group, or by adjustment for age and year of death. Further analyses revealed a statistically significant five-fold risk (95% CI = 2.3–10.8) associated with a particular group of physicians (doctors of osteopathic medicine). Recognizing that such a problem could be amenable to remediation through targeted education, we notified the Michigan Department of Public Health's Department of Vital Statistics. They followed-up with their own investigation by using a much larger sample of death records and confirmed our finding (personal communication with George Van Amburg).

In summary, our investigation of an excess of 44 deaths from COUS found: 1) approximately 25% was due to a previously recognized excess of mortality from malignant mesothelioma; 2) another 25% was attributable to our nosologists not having access to additional diagnostic information obtained by the states via querying

certifying physicians: and 3) the remaining 50% was due to the practices of a select group of physicians from neighboring Bay County.

With regard to the differential misclassification bias introduced by our lack of access to additional diagnostic information obtained by the states through querying, the problem could be avoided altogether if the underlying cause of death codes were made available from the National Death Index. Unfortunately, the contracts with State Vital Statistics offices (by which NCHS obtains the NDI records) currently permit only the release of date of death, state where the death occurred, and certificate number [Patterson and Bilgrad, 1986]. We would suggest that any arrangement for the NDI's release of cause of death codes provide for appropriate remuneration to the states and for protection of the confidential nature of the records.

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Letter to the Editor

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An investigation of excess cancer of other and unspecified sites among chemical workers

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Key words: death certificates, malignant mesothelioma, occupational cancer risk, chemical workers, Osteopaths, Michigan population

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